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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

FOLEY, SHANON A

ART UNIT	PAPER NUMBER
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1648

DATE MAILED: 07/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/989,933

Applicant(s)

CAO ET AL.

Examiner

Shanon Foley

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 March 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 30-59 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 35 and 37 is/are allowed.
- 6) ☒ Claim(s) 30,32-34,36 and 38-59 is/are rejected.
- 7) ☒ Claim(s) 31 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>10/4/4</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Upon further consideration of the prior art, new grounds of rejection are required.

Information Disclosure Statement

There was an IDS submitted October 4, 2004 that was inadvertently missed for consideration in the previous Office action. The references (also cited on page 9 of the specification), have been considered.

Specification

In response to the typo previously noted, applicant amended pages 2 and 5 to incorporate US Patent Nos. 6,168,942, 6,410,032 and 6,410,229. The discussion on pages 2 and 5 of the instant disclosure clearly reflects the subject matter of these patents (which claim priority to 60/107,908). Upon review, it is determined that the disclosures between each of the patents now listed and the provisional application are nearly identical. Therefore, it is concluded that "08/107,908" was an inadvertent typo and the incorporation of US Patent Nos. 6,168,942, 6,410,032 and 6,410,229 does not present new matter. It is noted that the same incorrect serial number is also present on page 15, line 11. Applicant is required to correct the typo throughout the disclosure.

Claim Objections

Claims 32, 34, 38, 43, 45 and 49 are objected to because the claims lack periods.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claims 30, 32-34, 36 and 38-59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention..

Claims 30, 32-34 and 42-45 recite "at least about". It is not clear what is intended by this phrase since 35 or 309 base pairs are "about" 36 or 310, respectively, but are not "at least" 36 or 310 base pairs. This rejection also affects all dependent claims.

These same claims are also rejected because it cannot be determined from the language recited how Npro is mutated since "at least" 36 or 310 base pairs of the 5' region remains intact. This language encompasses the entire, intact Npro gene. However, the claims also require that the Npro gene be mutated in such a way that an attenuated BVDV is produced. There is a clear discrepancy between structural scope claimed and the desired function.

There is a lack of antecedent basis in claim 36 regarding the dependency from claim 37 since the nucleic acid of the vector in claim 37 is not isolated from the vector, unless applicant intends for the vector of claim 36 to comprise the vector of claim 37. However, there is no support for this concept in the original disclosure. It is also noted that claim 36 depends from itself, rendering the limitations of the claim unclear. This rejection also affects claims 38-41.

There is also a lack of antecedent basis in claims 38, 47, 49, 55 and 57 with respect to dependency from claims 36 and 37 since vectors are not equivalent to the isolated nucleic acid molecules of claims 33-35. This rejection also affects claim 40, 51 and 52.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 30-34, 36 and 38-59 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an attenuated BVDV that has about 310 base pairs of the Npro gene intact, does not reasonably provide enablement for scope of mutations to Npro claimed or an intact Npro. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

As discussed above, the claims fail to define a structure of the intact Npro gene that remains in the attenuated BVDV genome. The claims encompass constructs comprising "at least" 310 base pairs of the 5' Npro region. While the claims encompass the entire, intact Npro gene, the claims also require that Npro be mutated to produce an attenuated BVDV. The disclosure exemplifies a mutated Npro that has about 310 base pairs intact from the 5' end (see page 6, lines 34- 36, page 7, lines 19-24, page 22, line 14 to page 23, line 8). The Npro coding region is 504 base pairs, see page 7, lines 19-24. Starting from position 310, there are 194 base pairs of the Npro gene that may be mutated. Mutations include substitution, deletion or insertion of one or more base pairs that results in inactivation of Npro to result in an attenuated virus with a reduced ability to replicate, see page 7, lines 1-8. However, the disclosure does not provide any guidance for what structural features downstream of position 310 are required to be mutated for the desired function of BVDV attenuation or how any single or group of nucleic acids downstream of 310 are required to be mutated to achieve the claimed effect. The disclosure must provide some evidence to support the assertions in the claims. Since there is no teaching in the prior art regarding partial deletion or mutating Npro from the 3' end to position 310, the skilled artisan would be unable to predict how to mutate the gene to achieve the desired

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attenuated phenotype beyond position 310 without some guidance provided from the instant disclosure. For these reasons, it is determined that an undue quantity of experimentation would be required of the skilled artisan to make the invention commensurate in the scope claimed.

With respect to the arguments presented that remain pertinent to the instant rejection, applicant argues that the area of the genome to be mutated is only a small area and that the skilled artisan would be able to predict and screen mutations that are likely to result in an inactive gene. Applicant also points to case law to support the argument. However, the law cited is irrelevant to the instant case since there is no parallel between identifying catalysts to produce hydroperoxides and mutating known nucleic acid residues within a viral genome to produce an inactivated gene, which results in an attenuated viral phenotype. While it is agreed that every enabled embodiment need not be described to support the claims, the disclosure must provide some guidance to the skilled artisan to practice the invention claimed. The disclosure has disclosed two species of attenuated BVDV that have an Npro gene with an intact 5' end. There is no discussion present in the specification or the art regarding the remaining residues of the Npro gene or what effect any of residues would have on attenuating phenotype or gene inactivation if any one or any combination were substituted, deleted, inserted or remained intact. Without some guidance, the skilled artisan would be unable to predict which nucleic acids within the 3' end of the Npro gene have an effect with respect to its function and subsequent virus attenuation, which are required elements recited in the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 30, 33, 36, 38-42, 44, 46, 47, 54 and 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Behrens et al. (Journal of Virology. 1998; 72 (3): 2364-2372).

The claims are drawn to an attenuated BVDV that has a mutated Npro gene comprising at intact region of at least about 36 base pairs and a sequence encoding a monomeric bovine ubiquitin between the 3'end of the mutated Npro gene and the 5'end of the viral core protein. The claims also encompass a method of making the construct, an immunogenic composition and a vaccine comprising the altered BVDV.

Behrens et al. teach a method of making a mutated BVDV that has a mutated Npro gene comprising at intact region of 126 base pairs at the 5'end and a sequence encoding a monomeric murine ubiquitin between the 3'end of the mutated Npro gene and the 5'end of the viral core protein, see "Construct of recombinant plasmids" on page 2365, Figure 5A and the paragraph bridging pages 2369-2370. The difference between the BVDV of Behrens et al. and the instant BVDV claimed is the animal species of ubiquitin used. However, Behrens et al. teach that any complete ubiquitin monomer can substitute for the proteolytic function of Npro, see the first full paragraph on page 2371. Therefore, substituting a bovine ubiquitin monomer in a bovine viral genome would have been a prima facie obvious alternative to the murine ubiquitin used by Behrens et al. Although Behrens et al. do not discuss administering the construct as an immunogenic composition, the mutated Npro/ubiquitin components in the mutated BVDV of Behrens et al. are obvious equivalents to the mutated Npro/ubiquitin components claimed.

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Allowable Subject Matter

Claim 31 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 35 and 37 are allowed.

The prior art does not teach or suggest nucleic acid sequences that encode SEQ ID NO: 11 or degenerate variants thereof that encode the same amino acid.

The prior art also does not teach or suggest inactivating the Npro gene of BVDV by leaving the extreme 5' end to nucleotide position number 310 intact to inactivate the gene. The closest prior art is US 6,410,299, US 6,916,477, US 6,410,032 and US 6,168,942. These patents discuss inactivating the Npro gene by deleting portions of the gene. However, the mutations described particularly encompass the 5' end with deletions from position 1-38, see claims 1-4 of '032, claims 1, 2 and 26 of (original, issued claim numbers) of '477, claims 1-9 of '299, claims 1-5 of '942, as well as Figures 1 and 2 and approximately column 2, line 46 to column 3, line 6 of each patent. Therefore, neither the species nor the genus of mutations to the Npro gene discussed in the prior art anticipate or render the instant species prima facie obvious.

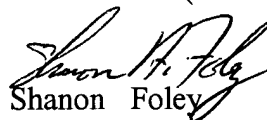
Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (571) 272-0898. The examiner can normally be reached on M-F 6:00 AM - 2:30 PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Shanon Foley
Primary Examiner
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